hypertensive patients (15 males and 3 females; 69 ± 5 years of age), on Captopril (25 mg b.i.d.; n = 11) or Enalapril (20 mg o.d.; n = 7) treatments. Half of the patients received ACEI + NAC (1800 mg/day), while the other half only received ACEI. After 21 days the therapeutical regimen was crossed and then another 21 day period was completed. Ambulatory blood pressure (BP) monitoring was performed at the end of each therapeutical regimen in each patient and the results of both measurements (ACEI vs ACEI + NAC) were compared. Decreases ($p < 0.05$) in 24 h BP and daytime BP were achieved with the association of NAC to ACEI. 24 h BP: 146 ± 5 vs 137 ± 4 (systolic BP) and 89 ± 3 vs 83 ± 4 (diastolic BP) mmHg. Daytime BP: 149 ± 6 vs 141 ± 4 (systolic BP) and 92 ± 4 vs 86 ± 3 (diastolic BP) mmHg. Significant differences were observed neither in nighttime BP nor between both ACEI treatments. In summary, the association of NAC to ACEI potentiates the antihypertensive effect of these drugs during daytime and in 24 hours BP in smoker hypertensives. This might be due to the protective effect of NAC on NO oxidation. Thus, supplementation of ACEI treatments with NAC may give additional advantages to smoking hypertensive patients.

11:30

741-5 Comparison of Circulating Von Willebrand Factor Levels and Acetylcholine Responsiveness as Markers of Endothelial Dysfunction in Hypertensive and Atherosclerotic Patients

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Either increased circulating levels of von Willebrand Factor (vWF), a glycoprotein secreted in greater amounts by a dysfunctional endothelium, or blunted vasorelaxation to intraarterial (i.a.) forearm infusion of acetylcholine (Ach), a nitric oxide-releasing muscarinic agonist, are frequently taken as evidence for endothelial dysfunction in both hypertension (*Ht*) and atherosclerosis (*Ath*). However, the relationship between the two indices and their relative sensitivity as markers of disease, is unknown. vWF levels (%, immunoenzymatic method) and the forearm blood flow (FBF, ml/min × dl^{-1}, strain-gauge plethysmography) response to i.a. Ach (7.5, 15 and 30 μg/min × 5 min each) were evaluated in i) 8 CONTROLS (*NOR*, age: 60 ± 12, $ASBPM_{24\text{-}hr}$: 129 ± 12), ii) 11 Normotensives With Atherosclerotic Peripheral Vascular Disease (PVD) (*NOR-ATH*, age: 54 ± 8, $ASBPM_{24\text{-}hr}$: 128 ± 9), iii) 10 Non Atherosclerotic Essential Hypertensives (*EH*, age: 56 ± 10, $ASBPM_{24\text{-}hr}$: 148 ± 12) and iv) 11 EH With Atherosclerotic PVD (*EH-ATH*, age: 60 ± 7, $ASBPM_{24\text{-}hr}$: 154 ± 9).

vWF was 95 ± 39 and 104 ± 15 in *NOR-ATH* and *EH-ATH* vs 70 ± 26 and 67 ± 29% in *NOR* and *EH* ($p < 0.005$ for *Ath* vs *non-Ath*); Ht carried no difference ($p < 0.5$). Maximum vasorelaxing response to Ach ($FBF_{30\ \mu g/min}/FBF_{basal}$) was 4.8 ± 2 and 5.9 ± 2.2 vs 6.4 ± 3.5 and 5.2 ± 2.3, respectively; the difference (*Ath* vs *non-Ath*: $p < 0.09$; *Ht* vs *non-Ht*: $p < 0.6$) was not significant.

Biochemical and pharmacological markers for endothelial dysfunction are not equivalent. vWF is a sensitive marker for atherosclerotic status; on the contrary, the forearm vasorelaxing response to i.a. Ach differentiated neither *Ath* nor *Ht* in this particular series.

11:45

741-6 A Localized Defect in the Phosphoinositol Pathway May Explain the Impaired Endothelial Nitric Oxide Activity in Hypertensive Patients

C. Cardillo, C.M. Kilcoyne, A.A. Quyyumi, R.O. Cannon, III, J.A. Panza. *NHLBI, Bethesda, MD, USA*

Patients with essential hypertension (HTs) have impaired endothelial nitric oxide (NO) activity. Although its mechanism is unknown, we have previously shown that the abnormality is not localized at the receptor or the G protein level. To investigate whether the endothelial dysfunction of HTs is related to a more distal defect in intracellular signal transduction, we studied the forearm blood flow response to intraarterial infusion of isoproterenol (ISO; 50–200 ng/min), a β_2 agonist that stimulates NO release through the G_s protein/cAMP pathway, and acetylcholine (Ach; 7.5–30 μg/min), an endothelial agonist that acts through the $G_{i/o}$/phosphoinositol pathway, in 12 normotensives (NTs) and 12 HTs. The infusion of ISO was repeated during the concurrent infusion of L-NMMA (4 μmol/min), a blocker of NO synthesis. The vasodilator response to ACh was significantly reduced in HTs compared to NTs (peak flow: 10.4 ± 4.6 vs. 14.4 ± 3.7 mL/min/dL; P = 0.008). However, the vasodilator effect of ISO was similar in NTs and HTs (peak flow: 14.4 ± 5.4 vs 13.5 ± 5 mL/min/dL; P = 0.56), and was significantly and equally blunted by L-NMMA in both groups (22 ± 15% in NTs vs 23 ± 16% in HTs; P = 0.83). The vasodilator response to sodium nitroprusside (0.8–3.2 μg/min), an exogenous NO donor, was similar in both groups and not modified by L-NMMA. Thus, in HTs with impaired endothelium-dependent vasodilation to ACh, the NO response to β_2-adrenergic stimulation is preserved. These findings suggest that the endothelial abnormality in hypertension is at least partly related to a defect in the pathway.

742 Atrial Arrhythmias

Tuesday, March 18, 1997, 10:30 a.m.–Noon
Anaheim Marriott, South Hall

10:30

742-1 Potential Pitfalls Using the P-wave Morphology in Leads aVL and V1 to Localize the Site of Origin of Atrial Tachycardias

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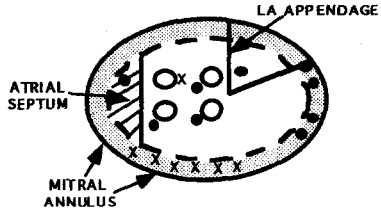
Preliminary reports suggest that the P-wave morphology on the 12 lead ECG can be used to localize the site of origin (*SOO*) of atrial tachycardias (*AT*). Specifically, a positive (+) P-wave in lead aVL during *AT* has been shown to predict the right atrium as the *SOO*, while a + P-wave in lead V1 during *AT* suggests a left atrial *SOO*. We report on the P-wave morphology of 16 left *AT* in 12 consecutive patients undergoing radiofrequency catheter ablation. Only one patient had multiple *AT*. Detailed mapping and localization of each *AT* was performed (Fig.). Ten of the *AT*'s were localized to the mitral valve annulus as indexed by fluoroscopy and amplitude of the ventricular electrogram recording. *Results:* The P-wave was + in lead aVL in 7 *AT*'s (*x*, in Fig.) and negative or isoelectric in 11 *AT*'s (•, in Fig.).



The P-wave was + in lead V1 for all of the *AT*'s. Six of the 7 *AT*'s with a + P-wave in aVL were localized to the inferomedial mitral valve annulus and demonstrated a similar P-wave precordial pattern characterized by a + P-wave in lead V1 and negative P-waves in leads V4–V6. The other *AT* with a + P-wave in aVL originated from adjacent to the right superior pulmonic vein and demonstrated a + P-wave in all precordial leads. *Conclusions:* A + P-wave in lead aVL during *AT* is not specific for a right atrial *SOO*. Left *AT*'s with a + P-wave in leads aVL and V1 appear to originate from either the inferomedial mitral annulus or right superior pulmonic vein region. A negative P-wave in leads V4–V6 further localizes the *SOO* to the inferomedial mitral annulus.

10:45

742-2 Body Surface Mapping of Counterclockwise and Clockwise Typical Atrial Flutter in Man

A. SippensGroenewegen, F.X. Roithinger, W.S. Ellis, M.D. Lesh. *University of California, San Francisco, CA, USA*

Typical atrial flutter (AFl) can be characterized as counterclockwise (CCW) or clockwise (CW) based on the direction of rotation along the tricuspid annulus. Although the 12-lead ECG P wave morphology of typical AFl is well known, the total body surface flutter wave distribution has not been reported. Therefore, 62-lead body surface mapping was performed in 9 pts during a total of 12 distinct spontaneous or induced episodes of typical AFl (mean cycle length 233 ± 20 msec). Structural heart disease was present in 5 pts. Temporary AV conduction block using adenosine was obtained when necessary to isolate the P wave from the QRS and T wave. Confirmation of CCW or CW typical AFl was performed by activation and entrainment mapping to demonstrate participation of the subeustachian sinus as a critical isthmus. A body surface P wave integral map was computed for each AFl episode. Analysis of the P wave integral maps included: 1) visual assessment of the potential distribution; and 2) quantitative map comparison for either the group of CCW or CW AFl episodes using a jack-knife procedure resulting in a mean correlation coefficient and SD to express the level of pattern uniformity within each group. *Results:* There were 6 CCW and 6 CW AFl episodes all demonstrating a dipolar P wave integral map pattern. Maps

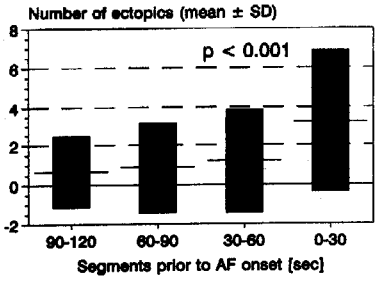
of CCW AFI displayed a characteristic pattern featuring a minimum at the lower left anterior thorax and a maximum at the upper right side of the sternum. In contrast, all maps of CW AFI showed the mirror image of the CCW AFI potential distribution with a minimum at the upper right side of the sternum and a maximum at the lower left or middle anterior torso. A higher degree of quantitative pattern uniformity was noted among CCW (r = 0.89 ± 0.04) as opposed to CW AFI P wave integral maps (r = 0.75 ± 13). *Conclusions:* CCW and CW typical AFI are characterized by a unique body surface P wave integral map pattern irrespective of the presence or absence of structural heart disease. These results may lead to the use of body surface mapping to distinguish typical from atypical forms of atrial flutter that do not use the subeustachian sinus.

11:00

742-3 Atrial Ectopic Activity Prior to the Onset of Paroxysmal Atrial Fibrillation

J.E.P. Waktare, K. Hnatkova, F.D. Murgatroyd, X. Baiyan, A.J. Camm, M. Malik. *St George's Hospital Medical School, London, England*

Introduction: Atrial ectopic beats may predispose to atrial fibrillation as alternating short and long cycles will increase dispersion of effective refractory period in the atrial myocardium, and analogous to the onset of VF, a critically timed ectopic may initiate AF. *Methods:* Episodes of AF lasting more than 30 sec were identified by a validated semi-automated method from a database of Holter tapes of patients with symptomatic paroxysmal AF. The 2 minutes segment prior to AF was analysed and the episode rejected if it contained any noise or artefact. Short cycles (ectopic beats) were defined as those RR intervals which had a duration less than 80% of the median of the previous 10 beats, and long cycles (usually due to a compensatory pause) as greater than 120%. Relative numbers of abnormal duration cycles were compared in the four 30 sec segments before onset of AF. *Results:* A highly significant increase in the number of ectopics was seen in the 30 seconds immediately prior to the onset of AF ($p < 0.001$, one sample non-parametric Wilcoxon test), with a non-significant trend of increasingly frequent ectopics in earlier segments.



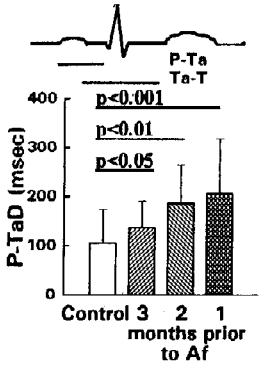
Conclusion: The number of ectopics increases progressively prior to the onset of AF, particularly during the last 30 sec. The variation in number of ectopics is however very wide.

11:15

742-4 Exaggerated Dispersion of P-Ta and Ta-T Interval as a Predictor of Atrial Fibrillation

G. Cui, G.C. Fonarow, H. Laks, L. Sen. *UCLA Medical Center, UCLA, School of Medicine, Los Angeles, CA, USA*

Experimental animal studies have shown that atrial fibrillation (Af) is based on multiple wavelet reentry. Dispersion of refractoriness is considered to favor induction and maintenance of reentrent arrhythmias. Therefore, analysis of the atrial repolarization waves in ECG is of theoretical as well as practical interest, especially in relation to atrial arrhythmias and atrial conduction disturbance. We analyzed 75 12-leads ECGs recorded in 33 patients 2 hours to 6 months (mean 25 days) prior to the onset of Af compared with that from 50 normal subjects. The isoelectric line was used for determining the P-Ta and Ta-T (from the end of P wave to the beginning of T wave). QRS, RR intervals and P-Ta dispersion (P-TaD) and Ta-T dispersion (Ta-TD) were also measured. The mean P-Ta interval was significantly prolonged in ECGs recorded from patients prior to the onset of Af than that in normal controls (163 ± 26 vs. 152 ± 20 msec; $p < 0.001$), but the mean Ta-T interval was not changed ($p > 0.05$). The P-TaD and Ta-TD were gradually increased and it were almost 2 to 3 fold greater than that in controls (207 ± 112 vs. 106 ± 68 msec; $p < 0.001$ and 491 ± 131 vs. 184 ± 68 msec; $p < 0.001$, respectively) before the onset of Af. QRS, RR and QT intervals were not significantly different ($p > 0.05$). Significant increase of the left atrial diameter was only found in 8 out of 33 patients by ECG and/or Echocardiography. These results indicate that significant increases in P-TaD and Ta-TD during sinus rhythm may reflect intrinsic atrial conduction disturbance, and might be used as a predictor of Af.



11:30

742-5 Value of Signal Averaged P-Wave Duration (SAPWD) in Predicting Atrial Fibrillation After Thoracic Surgery

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Sustained atrial fibrillation (AF) after thoracic surgery has been associated with increased morbidity and hospital stay. We prospectively examined the predictive value of a prolonged preoperative SAPWD for postoperative AF in 166 patients having major thoracic surgery known to be at high risk for AF (n = 105, group – HR), and those undergoing minor thoracic or abdominal/peripheral operations known to be at low risk for AF (n = 61, group – LR). Excluded were patients with prior AF or those receiving β-blockers or antiarrhythmic drugs. SAPWD was recorded before surgery using a sinus P-wave template. SAPWD was measured visually from a filtered vector composite of three orthogonal leads by consensus of 2 investigators unaware of patient end points. Patients were followed for symptomatic AF during hospitalization.

Results: AF occurred in 16/105 (15%) HR-patients and in 0/61 (0%) LR-patients during hospitalization. HR patients with AF were older than other HR but not LR patients (* p = 0.05, table). There were no differences among the groups in male sex, SAPWD or in the incidence of SAPWD > 140 ms (table). The incidence of left ventricular hypertrophy on preoperative ECG was low and similar among the groups.

Variable	HR-AF (n = 16)	HR-No AF (n = 89)	LR (n = 61)
Age, yr.	66 ± 9*	63 ± 10	63 ± 13
Male, no. (%)	12 (75)	56 (63)	40 (66)
SAPWD, ms	147 ± 19	147 ± 15	144 ± 15
SAPWD > 140 ms, no. (%)	9 (56)	56 (63)	37 (61)

Conclusions: As opposed to cardiac surgery, the presence of preexisting atrial electrical substrate (prolonged SAPWD) is not associated with risk of new onset AF in non-cardiac thoracic surgery. Consistent with other reports, older age was a risk factor for AF.

11:45

742-6 Change in Mean RR Interval Prior to the Onset of an Episode of Atrial Fibrillation

K. Hnatkova, J.E.P. Waktare, F.D. Murgatroyd, X. Baiyan, A.J. Camm, M. Malik. *St George's Hospital Medical School, London, England*

Introduction: In some patients, episodes of paroxysmal atrial fibrillation (PAF) are induced by high vagal tone, or less frequently, high sympathetic tone, but whether this occurs in an unselected population is unknown. 'Vagal AF' would be expected to be associated with progressive slowing of an already slow heart rate, and the converse to be true of sympathetic onset. *Methods:* From a database of Holter tapes in patients with PAF who were part of the CRAFT studies, all noise free episodes of AF lasting more than 30 sec were identified. A comparison was made between the mean RR interval during the 30 sec immediately before the onset of AF with that during the interval 120 sec to 90 sec prior to onset. As the frequency of ectopic beats increases immediately prior to the onset of AF and may have effected results, all cycles of abnormal duration were excluded.

Results: 231 episodes from 33 recordings (26 different patients) fulfilled the criteria and the results shown on the graph. The light and dark areas